(FILE 'HOME' ENTERED AT 14:22:42 ON 18 JUN 1999)

FILE 'SCISEARCH, MEDLINE, CAPLUS, BIOSIS, CANCERLIT, AGRICOLA, GENBANK'
ENTERED AT 14:22:50 ON 18 JUN 1999

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L1          9926 S ECDYSONE
L2          1144 S L1 AND RECEPTOR
L3             2 S L2 AND (GENE TRANSFER)
L4           106 S L2 AND MAMMAL?
L5            73 S L4 AND EXPRESSION
L6            20 S L5 AND INDUCIBLE
L7            16 DUP REM L6 (4 DUPLICATES REMOVED)
L8            16 SORT L7 PY
L9           229 S L2 AND INDUCIBLE
L10           23 S L9 AND MAMMAL?
L11           19 DUP REM L10 (4 DUPLICATES REMOVED)
L12           19 SORT L11 PY
L13           25 S L1 AND (GENE THERAPY)
L14           16 DUP REM L13 (9 DUPLICATES REMOVED)
L15           25 SORT L13 PY
L16           16 SORT L14 PY
L17            0 S L2 AND VPECR
                 E EVAN RONALD/AU
L18            0 S E3
                 E EVANS RONALD/AU
L19           13 S E3
L20           12 DUP REM L19 (1 DUPLICATE REMOVED)
L21           12 SORT L20 PY
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=> d l8 3 all

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 1999 ACS
AN 1994:209524 CAPLUS
DN 120:209524
TI Binding of members of the steroid/thyroid superfamily of **receptors** with the ultraspiracle **receptor**
IN Evans, Ronald M.; McKeown Michael B.; Oro, Anthony E.; Segraves, William A.; Yao, Tso Pang
PA Salk Institute for Biological Studies, USA
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C07K015-06
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 3, 12, 13
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9401558	A2	19940120	WO 93-US6296	19930701
	WO 9401558	A3	19940526		
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9347697	A1	19940131	AU 93-47697	19930701
	JP 08501211	T2	19960213	JP 93-503431	19930701
	EP 804568	A2	19971105	EP 94-904904	19930701
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, PT, IE				
PRAI	US 92-907908	19920702			
	WO 93-US6296	19930701			

AB Members of the steroid/thyroid superfamily of **receptors** can interact with the insect-derived ultraspiracle (usp) **receptor**, to form multimerics. The system is useful in achieving high-level **expression** of exogenous genes in transgenic systems using a steroid hormone-responsive system (no data). The interaction of a member of the steroid/thyroid superfamily of **receptors** with dimerization domain of the ultraspiracle **receptor** modulates the

ability of the steroid/thyroid **receptor** to transactivate transcription of genes regulated by steroid or thyroid hormones in the presence of the cognate ligand for the **receptor**. The usp **receptor** was prepd. by in vitro translation of the mRNA and shown to increase the binding of the retinoic acid **receptor** the .beta.RARE element. Mobility shift expts. demonstrated that the usp **receptor** formed heterodimers with the **mammalian** nuclear **receptors** TR.beta., VDR, and PPAR and affected their binding to the cognate regulatory element. A complex between usp and the **ecdysone receptor** had a very high affinity for DNA with the binding of the complex for DNA correlating with the functionality of the **ecdysone receptor** binding site on the target sequence.

ST ultraspiracle steroid **receptor** heterodimer; thyroid **receptor** ultraspiracle heterodimer

IT Genetic element
RL: BIOL (Biological study)
(PPAR-responsive element, **receptor** binding to, complex with ultraspiracle **receptor** for stimulation of)

IT Gene
RL: BIOL (Biological study)
(exogenous, regulation of **expression** of, ultraspiracle **receptor** complexes with steroid/thyroid **receptor** for)

IT Deoxyribonucleic acid sequences
(of ultraspiracle gene of Drosophila melanogaster)

IT Protein sequences
(of ultraspiracle gene product of Drosophila melanogaster)

IT Transcription, genetic
(steroid/thyroid hormone **receptor**-dependent, stimulation of, formation of complex with ultraspiracle **receptor** in)

IT Drosophila melanogaster
(ultraspiracle gene product of, interaction with steroid/thyroid **receptors** of)

IT **Receptors**
RL: BIOL (Biological study)
(ultraspiracle, complexes with steroid/thyroid **receptors**, formation of, increased DNA binding by, regulation of **expression** of exogenous genes by)

IT **Receptors**
RL: BIOL (Biological study)
(PPAR (peroxisome proliferator-activated **receptor**), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT **Receptors**
RL: BIOL (Biological study)
(RAR-.alpha. (retinoic acid **receptor** .alpha.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Retinoids
RL: BIOL (Biological study)
(RAR-.alpha. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT **Receptors**
RL: BIOL (Biological study)
(RAR-.beta. (retinoic acid **receptor** .beta.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Retinoids
RL: BIOL (Biological study)
(RAR-.beta. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT **Receptors**
RL: BIOL (Biological study)
(RAR-.gamma. (retinoic acid **receptor** .gamma.), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Retinoids
RL: BIOL (Biological study)
(RAR-.gamma. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Genetic element
RL: BIOL (Biological study)
(RARE (retinoic acid-responsive element), .beta.-, **receptor**

binding to, complex with ultraspiracle **receptor** for stimulation of)

IT **Receptors**
RL: BIOL (Biological study)
(TR (thyroid/steroid hormone **receptor**), ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Thyroid hormones
(TR **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Steroids, biological studies
RL: BIOL (Biological study)
(TR **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Genetic element
RL: BIOL (Biological study)
(TRE (thyroid hormone-responsive element), **receptor** binding to, complex with ultraspiracle **receptor** for stimulation of)

IT **Receptors**
RL: BIOL (Biological study)
(ecdysteroid, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Genetic element
RL: BIOL (Biological study)
(promoter, tissue-specific, **expression** of exogenous genes from, steroid-responsive element and steroid/thyroid and ultraspiracle **receptors** in)

IT Ecdysteroids
(**receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Genetic element
RL: BIOL (Biological study)
(steroid-responsive element, exogenous gene under control of, regulated **expression** of, ultraspiracle **receptor** complexes with steroid/thyroid **receptor** for)

IT **Receptors**
RL: BIOL (Biological study)
(thyroid hormone .alpha., ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT **Receptors**
RL: BIOL (Biological study)
(thyroid hormone .beta., ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Gene, animal
RL: BIOL (Biological study)
(ultraspiracle, in **expression** of exogenous genes in steroid-**inducible** system)

IT **Receptors**
RL: BIOL (Biological study)
(vitamin D, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Genetic element
RL: BIOL (Biological study)
(vitamin D-responsive element, **receptor** binding to, complex with ultraspiracle **receptor** for stimulation of)

IT Thyroid hormones
RL: BIOL (Biological study)
(.alpha. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT Thyroid hormones
RL: BIOL (Biological study)
(.beta. **receptors**, ultraspiracle **receptor** complexes with, formation of, increased DNA binding by)

IT 138263-72-6, Protein (Drosophila melanogaster gene ultraspiracle reduced)
RL: PRP (Properties)
(amino acid sequence of, formation of complexes with steroid/thyroid **receptor** of, stimulation of gene **expression** by)

IT 154173-85-0
RL: PRP (Properties)
(amino acid sequence of, relationship to RXR **receptors** of)

IT 153679-02-8 153679-03-9 153679-04-0 153679-05-1
RL: BIOL (Biological study)
(**ecdysone receptor** binding to, stimulation by

ultraspiracle **receptor** of)

IT 138263-42-0
RL: PRP (Properti[redacted]
(nucleotide sequence of)

IT 153678-98-9 153678-99-0 153679-00-6 153679-01-7
RL: BIOL (Biological study)
(**receptor** binding to, stimulation by ultraspiracle **receptor** of)

L16 ANSWER 7 OF 16 CAPLUS COPYRIGHT 1999 ACS
AN 1998:25131 CAPLUS
DN 128:98563
TI Modular assembly retroviral vectors for high level and ligand-modulatable gene expression
IN Gage, Fred H.; Suhr, Steven T.
PA Salk Institute for Biological Studies, USA; Gage, Fred H.; Suhr, Steven T.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N043-04
ICS C12N005-00; C12N015-00; C12P021-00
CC 3-2 (Biochemical Genetics)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9748277	A1	19971224	WO 97-US8805	19970522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732121	A1	19980107	AU 97-32121	19970522
PRAI US 96-677025	19960620			
WO 97-US8805	19970522			

AB In accordance with the present invention, novel retroviral vectors contg. modified long terminal repeats (LTRs) which enable high level and ligand-modulatable expression of a desired gene product, even after prolonged periods of cellular quiescence, have been designed and constructed. Invention vectors overcome proviral transcriptional inactivation which occurs in cultured primary cells that are growth arrested due to environmental constraints such as contact inhibition and/or nutrient starvation. Invention vectors represent a class of retroviral vectors in which LTR-promoted proviral expression in infected cells may be maintained or increased, even in situations generally considered to be non-permissive for retroviral vectors. The family of retroviral vectors, collectively referred to as MARVs (for modular assembly retroviral vectors), are designed with LTR promoters that respond to specific constitutive or ligand-dependent transcription factors encoded by nucleic acids which have been introduced into the recombinant retroviral vectors. Three general elements combine to form MARV vectors: (1) native or mutated LTRs contg. regulatory elements responsive to a transactivator; (2) transactivator(s) optionally modified to provide a user-defined level of expression in the absence of ligand and higher-level expression in the presence of ligand; and (3) retroviral packaging signal. The first generation of MARV vectors were designed to respond to insect hormones (ecdysteroids) to stimulate transcription from the viral LTR. Examples of receptor complexes for ecdysteroids are composed of the Drosophila **ecdysone** receptor and the human retinoid X receptor or the Drosophila ultraspiracle receptor. A two-plasmid system is typically provided with antibiotic resistance markers, which enable the selection and characterization of infected cells in vitro. The co-functioning partner, referred to as MARSHA, is designed to encode a heterologous gene and a second antibiotic resistance gene.

ST retrovirus vector MARV MARSHA gene expression

IT Genetic elements
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(HRE (hormone-responsive element); modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Plasmid vectors
Retroviral vectors

(MARV and MARSHA; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Steroid receptors
Thyroid hormone receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(TR (thyroid/steroid hormone receptor); modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Genetic elements
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**ecdysone**-responsive element; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Transgenes
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(expression; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Hormone receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(juvenile hormone, ultraspiracle; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Gene expression
Gene therapy
(modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Ecdysteroid receptors
Ecdysteroids
LTR (long terminal repeat)
Retinoid X receptor .alpha.
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Genetic elements
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(packaging signal; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT Antibiotic resistance
(selection vectors for; modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

IT 60-54-8, Tetracycline 38778-30-2, Muristerone A 84371-65-3, RU486
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(modular assembly retroviral vectors for high level and ligand-modulatable gene expression)

=> d l16 4 all

L16 ANSWER 4 OF 16 CAPLUS COPYRIGHT 1999 ACS
AN 1997:72295 CAPLUS
DN 126:85631
TI A gene switch comprising an insect **ecdysone** receptor or fusion product allows gene control by external chemical inducer and has agricultural and pharmaceutical applications
IN Jepson, Ian; Martinez, Alberto; Greenland, Andrew James
PA Zeneca Limited, UK; Jepson, Ian; Martinez, Alberto; Greenland, Andrew James
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS C12N015-85; C12N015-62; C07K014-72; C07K019-00; C12N005-10; A61K038-16
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 5, 10, 11, 12, 13
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9637609	A1	19961128	WO 96-GB1195	19960520

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

CA 2219121	AA	19961128	CA 96-2219121	19960520	
AU 9657716	A1	19961211	AU 96-57716	19960520	
EP 828829	A1	19980318	EP 96-914309	19960520	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

CN 1191568	A	19980826	CN 96-195739	19960520	
JP 11506319	T2	19990608	JP 96-535473	19960520	
NO 9705419	A	19980122	NO 97-5419	19971125	

PRAI GB 95-10759 19950526
GB 95-13882 19950707
GB 95-17316 19950824
GB 96-5656 19960318
WO 96-GB1195 19960520

AB The invention relates to an insect steroid receptor protein which is capable of acting as a gene switch which is responsive to a chem. inducer enabling external control of the gene. The Heliothis virescens **ecdysone** receptor and the Spodoptera exigua **ecdysone** receptor or glucocorticoid receptor can be used. Expression of insect hormone receptors in plant, fungus, bacteria, or mammal can be useful. Plasmid constructs encoding insect hormone receptor fusion proteins with transactivator proteins of other sources are also included. Various promoters in plasmid constructs are included in further variations.

ST **ecdysone** receptor gene switch application; Heliothis **ecdysone** receptor gene switch application; transcription factor fusion **ecdysone** receptor application; Spodoptera **ecdysone** receptor gene switch application; insect **ecdysone** receptor gene switch application

IT Genetic elements
RL: AGR (Agricultural use); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HRE (hormone-responsive element); gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(TEV-8; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(TEV-B112; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(TEVVP16-3; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT GAL4 transcription factor
VP16 transcription factor
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion products; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT RNA formation factors
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene alcR, fusion products; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Animal cells
Bacteria (Eubacteria)
Corn
Fungi
Gene therapy

Genetic engineering
Heliothis virescen
Insect (Insecta)
Mammal (Mammalia)
Plant (Embryophyta)
Plasmid vectors
Protein sequences
Saccharomyces cerevisiae
Spodoptera exigua
Tobacco
cDNA sequences
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Ecdysteroids
Glucocorticoids
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Ecdysteroid receptors
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Glucocorticoid receptors
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Promoter (genetic element)
RL: AGR (Agricultural use); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(p221.10GRE6; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(p221.9GRE6; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pJRIES1; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pJRIES2; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pJRIES3; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pJRIES4; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF6GREcRS; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF6GRHEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has

agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF6GRVP16HEc[redacted]gene switch comprising insect **ecdys**[redacted] receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF6HG1PAT; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF7GREcRS; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF7GRHEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pMF7GRVP16HEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pSW GRE4; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pcDNA3GRHecR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Plasmid vectors
(pcDNA3GRVP16HEcR; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT Gene regulation
(switch; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT 185569-20-4P 185569-21-5P
RL: AGR (Agricultural use); BPN (Biosynthetic preparation); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

IT 185530-39-6 185530-40-9 185530-41-0 185569-19-1
RL: AGR (Agricultural use); BPR (Biological process); BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence; gene switch comprising insect **ecdysone** receptor or fusion product allows gene control by external chem. inducer and has agricultural and pharmaceutical applications)

L8 ANSWER 5 OF 16 SCISEARCH COPYRIGHT 1999 ISI (R)

TI **ECDYSONE-INDUCIBLE** GENE-**EXPRESSION** IN **MAMMALIAN**-CELLS AND TRANSGENIC MICE

SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (16 APR 1996) Vol. 93, No. 8, pp. 3346-3351.
ISSN: 0027-8424.

AU NO D; YAO T P; EVANS R M (Reprint)

AB During metamorphosis of Drosophila melanogaster, a cascade of morphological changes is triggered by the steroid hormone 20-OH **ecdysone** via the **ecdysone receptor**, a member of the nuclear **receptor** superfamily, In this report, we have transferred insect hormone responsiveness to **mammalian** cells by the stable **expression** of a modified **ecdysone receptor** that regulates an optimized **ecdysone** responsive promoter. Inductions reaching 4 orders of magnitude have been achieved upon treatment with hormone, Transgenic mice expressing the modified **ecdysone receptor** can activate an integrated **ecdysone** responsive promoter upon administration of hormone. A comparison of tetracyline-based and **ecdysone**-based **inducible** systems reveals the **ecdysone** regulatory system exhibits lower basal activity and higher inducibility. Since **ecdysone** administration has no apparent effect on **mammals** , its use for regulating genes should be excellent for transient **inducible expression** of any gene in transgenic mice and for gene therapy

L8 ANSWER 3 OF 16 CAPLUS COPYRIGHT 1999 ACS

TI Binding of members of the steroid/thyroid superfamily of **receptors** with the ultraspiracle **receptor**

SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2

IN Evans, Ronald M.; McKeown Michael B.; Oro, Anthony E.; Segraves, William A.; Yao, Tso Pang

AB Members of the steroid/thyroid superfamily of **receptors** can interact with the insect-derived ultraspiracle (usp) **receptor**, to form multimerics. The system is useful in achieving high-level **expression** of exogenous genes in transgenic systems using a steroid hormone-responsive system (no data). The interaction of a member of the steroid/thyroid superfamily of **receptors** with dimerization domain of the ultraspiracle **receptor** modulates the ability of the steroid/thyroid **receptor** to transactivate transcription of genes regulated by steroid or thyroid hormones in the presence of the cognate ligand for the **receptor**. The usp **receptor** was prepd. by in vitro translation of the mRNA and shown to increase the binding of the retinoic acid **receptor** the .beta.RARE element. Mobility shift expts. demonstrated that the usp **receptor** formed heterodimers with the **mammalian** nuclear **receptors** TR.beta., VDR, and PPAR and affected their binding to the cognate regulatory element. A complex between usp and the **ecdysone receptor** had a very high affinity for DNA with the binding of the complex for DNA correlating with the functionality of the **ecdysone receptor** binding site on the target

L8 ANSWER 1 OF 16 SCISEARCH COPYRIGHT 1999 ISI (R)
TI ECDYSTEROID-DEPENDENT REGULATION OF GENES IN **MAMMALIAN**-CELLS BY A DROSOPHILA **ECDYSONE RECEPTOR** AND CHIMERIC TRANSACTIVATORS
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (15 JUL 1992) Vol. 89, No. 14, pp. 6314-6318.
ISSN: 0027-8424.
AU CHRISTOPHERSON K S; MARK M R; BAJAJ V; GODOWSKI P J (Reprint)
AB Steroid **receptors** are members of a large family of transcription factors whose activity is tightly regulated by the binding of their cognate steroid ligand. **Mammalian** steroid hormone **receptors** have been exploited to obtain the regulated **expression** of heterologous genes in **mammalian** cells. However, the utility of these systems in cultured cells and transgenic animals is limited by the presence of endogenous steroids and their **receptors**. We show that a Drosophila **ecdysone receptor** can function in cultured **mammalian** cells as an ecdysteroid-dependent transcription factor. The activity of the **ecdysone receptor** was not induced by any of the **mammalian** steroid hormones tested. The DNA-binding and transactivation activities of viral, **mammalian**, or bacterial proteins were rendered ecdysteroid-dependent when fused to the ligand-binding domain of the **ecdysone receptor**. The **ecdysone receptor** may prove useful in selectively regulating the **expression** of endogenous or heterologous genes in

L8 ANSWER 10 OF 16 MEDLINE

TI **Mammalian expression** of transmembrane **receptors** for pharmaceutical applications.

SO BIOCHEMICAL SOCIETY TRANSACTIONS, (1998 Nov) 26 (4) 699-704. Ref: 26
Journal code: E48. ISSN: 0300-5127.

AU Rhodes A D; Bevan N; Patel K; Lee M; Rees S

AB Three **mammalian expression** systems suitable for expressing recombinant **receptors** have been described. Each is suited to a different aspect of the study of **receptors** and their behaviour. IRES-based vectors are ideal for creating stable **mammalian** cell lines suitable for screening **receptors** using a signalling readout. Unlike traditional vectors they result in almost 100% of cell lines generated expressing a particular **receptor**, thus increasing the efficiency of cell line generation and increasing the chance of higher **expression**-level cell lines being generated. They may also be utilized to express more than one protein of interest, for example it is possible to co-express a particular **receptor** with a particular signalling protein or trafficking protein from a single RNA, thus ensuring that both are expressed simultaneously in the same cell. The **ecdysone-inducible expression** system is ideal for studying **receptor** signalling and behaviour. It is possible to alter **receptor expression** levels in an identical cellular background thus making it possible to study phenomena such as constitutive **receptor** activity in the absence of agonist. The SFV **expression** system is ideal for expressing **receptors** at high levels of a **mammalian** cell. It is thus a good system for purifying **receptors** for structural analysis and for providing material for binding assays. All of the **expression** systems described above have been demonstrated to express seven-transmembrane **receptors**

12 ANSWER 14 OF 19 BIOSIS COPYRIGHT 1999 BIOSIS
TI Generation of transgenic mice with expression of the **ecdysone inducible** system in the central nervous system.
SO Society for Neuroscience Abstracts, (1998) Vol. 24, No. 1-2, pp. 71. Meeting Info.: 28th Annual Meeting of the Society for Neuroscience, Part 1 Los Angeles, California, USA November 7-12, 1998 Society for Neuroscience . ISSN: 0190-5295.
AU Kostich, W. A. (1); Neal, R. G.; Dinchuk, J. E.; Focht, R. J.; Margolis, F. I.; Largent, B.

L12 ANSWER 13 OF 19 MEDLINE
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12 ANSWER 2 OF 19 SCISEARCH COPYRIGHT 1999 ISI (R)
TI ECDYSTEROID-DEPENDENT REGULATION OF GENES IN **MAMMALIAN**-CELLS BY A DROSOPHILA **ECDYSONE RECEPTOR** AND CHIMERIC TRANSACTIVATORS
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (15 JUL 1992) Vol. 89, No. 14, pp. 6314-6318. ISSN: 0027-8424.
AU CHRISTOPHERSON K S; MARK M R; BAJAJ V; GODOWSKI P J (Reprint)
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L16 ANSWER 7 OF 16 CAPLUS COPYRIGHT 1999 ACS
TI Modular assembly retroviral vectors for high level and ligand-modulatable gene expression
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
IN Gage, Fred H.; Suhr, Steven T.
AB In accordance with the present invention, novel retroviral vectors contg. modified long terminal repeats (LTRs) which enable high level and ligand-modulatable expression of a desired gene product, even after prolonged periods of cellular quiescence, have been designed and constructed. Invention vectors overcome proviral transcriptional inactivation which occurs in cultured primary cells that are growth arrested due to environmental constraints such as contact inhibition and/or nutrient starvation. Invention vectors represent a class of retroviral vectors in which LTR-promoted proviral expression in infected cells may be maintained or increased, even in situations generally considered to be non-permissive for retroviral vectors. The family of retroviral vectors, collectively referred to as MARVs (for modular assembly retroviral vectors), are designed with LTR promoters that respond to specific constitutive or ligand-dependent transcription factors encoded by nucleic acids which have been introduced into the recombinant retroviral vectors. Three general elements combine to form MARV vectors: (1) native or mutated LTRs contg. regulatory elements responsive to a transactivator; (2) transactivator(s) optionally modified to provide a user-defined level of expression in the absence of ligand and higher-level expression in the presence of ligand; and (3) retroviral packaging signal. The first generation of MARV vectors were designed to respond to insect hormones (ecdysteroids) to stimulate transcription from the viral LTR. Examples of receptor complexes for ecdysteroids are composed of the Drosophila **ecdysone** receptor and the human retinoid X receptor or the Drosophila ultraspiracle receptor. A two-plasmid system is typically provided with antibiotic resistance markers, which enable the selection and characterization of infected cells in vitro. The co-functioning partner, referred to as MARSHA, is designed to encode a heterologous

L16 ANSWER 4 OF 16 CAPLUS COPYRIGHT 1999 ACS
TI A gene switch comprising an insect **ecdysone** receptor or fusion product allows gene control by external chemical inducer and has agricultural and pharmaceutical applications
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
IN Jepson, Ian; Martinez, Alberto; Greenland, Andrew James
AB The invention relates to an insect steroid receptor protein which is capable of acting as a gene switch which is responsive to a chem. inducer enabling external control of the gene. The Heliothis virescens **ecdysone** receptor and the Spodoptera exigua **ecdysone** receptor or glucocorticoid receptor can be used. Expression of insect hormone receptors in plant, fungus, bacteria, or mammal can be useful. Plasmid constructs encoding insect hormone receptor fusion proteins with transactivator proteins of other sources are also included. Various promoters in